

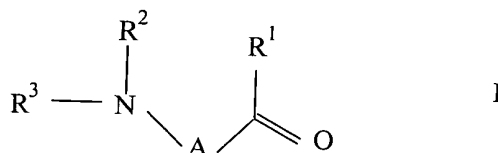
### Insecticide and Method of Controlling Insects

5 The invention relates to insecticidal compounds and compositions for controlling insecticides and to a method of controlling insects using the insecticidal compounds and compositions.

10 Insecticides are chemicals that are used to control damage or annoyance from insects. Control of insects may be achieved by oral ingestion of stomach poisons, contact poisons that penetrate the cuticle or fumigants that penetrate the respiratory system.

15 The wide use of insecticides particularly in crop protection has lead to the emergence of resistant insects. There is a need for new types of insecticides which are safe to use.

The invention provides an insecticidal compound of Formula I



20 and the agriculturally acceptable salts thereof, wherein:

R<sup>1</sup> is selected from the group consisting of:

25 the group OR<sup>5</sup> wherein R<sup>5</sup> is selected from the group consisting of hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclic and substituted heterocyclic;

30 the group -NR<sub>6</sub>OH wherein R<sup>6</sup> is selected from the group consisting of hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, carbocyclic and substituted carbocyclic;

the group  $\text{NR}^7\text{R}^8$  wherein  $\text{R}^7$  and  $\text{R}^8$  are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, aryl, substituted aryl and carbocyclic; and

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the group wherein  $\text{R}^1$  is linked to  $\text{R}^2$  to form a diradical bridging group;

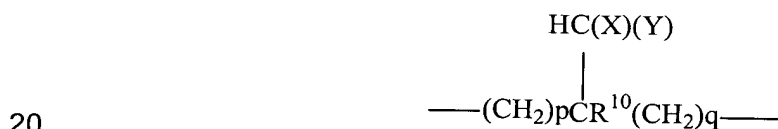
$\text{R}^2$  and  $\text{R}^3$  are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, carbocyclic, substituted carbocyclic, aryl, substituted aryl, acyl and substituted acyl; and

10

A is a diradical linking group which has a molecular weight of preferably less than 200 and more preferably less than 100.

15 The compounds include the agriculturally acceptable salts of compounds of formula I such as the salts formed at the amine moiety, phosphonic acid moiety carboxylic acid moiety and mixtures thereof.

A is preferably a diradical group of formula



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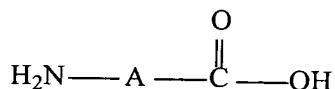
wherein the groups  $\text{R}^{10}$ , X and Y are independently selected from the group consisting of hydrogen, alkyl, thiol, hydroxy, thioalkyl, alkoxy, substituted alkyl, carbocyclic, substituted carbocyclic, heterocyclic and substituted heterocyclic; and more preferably  $\text{R}^{10}$  is hydrogen and X and Y are independently selected from the group consisting of hydrogen,  $\text{C}_1$  to  $\text{C}_6$  alkyl, thiol, hydroxy,  $\text{C}_1$  to  $\text{C}_6$  thioalkyl, aryl, substituted aryl,  $\text{C}_1$  to  $\text{C}_6$  alkoxy, substituted  $\text{C}_1$  to  $\text{C}_6$  alkyl,  $\text{C}_4$  to  $\text{C}_6$  carboxylic substituted  $\text{C}_4$  to  $\text{C}_6$  heterocyclic and substituted  $\text{C}_4$  to  $\text{C}_6$  heterocyclic;

25

p and q are selected from zero, 1, 2 and 3.

30

The divalent group "A" may be a group wherein the formula



- is a naturally occurring amino acid such as alanine, valine leucine, isoleucine, phenylalanine, tyrosine, tryptophan, serine, threonine, methionine, cysteine, pyrroline, hydroxy pyrroline, lysine and histidine.

Preferred A is selected from the group wherein  $\text{R}^{10}$  is hydrogen, p and q are zero and X and Y are as defined above.

- In more the preferred A group X is selected from the group consisting of hydrogen and  $\text{C}_1$  to  $\text{C}_6$  alkyl and Y is selected from the group consisting of hydrogen,  $\text{C}_1$  to  $\text{C}_6$  alkyl and phenyl.

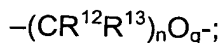
It is preferred that the substituent  $\text{R}^1$  is selected from the group consisting of

the group  $\text{OR}^5$  wherein  $\text{R}^5$  is selected from the group consisting of hydrogen, alkyl, haloalkyl, aryl substituted alkyl, heterocyclic, heterocyclic substituted with alkyl wherein the alkyl is optionally further substituted with hydrocarbyloxy such as  $\text{C}_1$  to  $\text{C}_4$  alkoxy;

the group  $\text{NR}_6\text{OH}$  wherein  $\text{R}^6$  is selected from the group consisting of hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, carbocyclic and substituted carbocyclic;

- the group  $\text{NR}^7\text{R}^8$  wherein  $\text{R}^7$  and  $\text{R}^8$  are independently selected from hydrogen and  $\text{C}_1$  to  $\text{C}_6$  alkyl; and

the group wherein  $\text{R}^1$  is linked to  $\text{R}^2$  to form a bridging group  $-\text{R}^2-\text{R}^1-$  of formula



wherein n is 1 or 2, q is zero or 1 and  $\text{R}^{12}$  and  $\text{R}^{13}$  are independently selected from hydrogen, halogen, alkyl and haloalkyl.

More preferred  $R^1$  is selected from the group consisting of

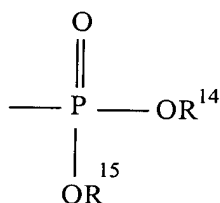
the group  $OR^5$  wherein  $R^5$  is selected from the group consisting of hydrogen,  
 5 alkyl, haloalkyl, aralkyl and alkylaryl and wherein more preferred  $R^5$  is  
 hydrogen,  $C_1$  to  $C_6$  alkyl, halogenated  $C_1$  to  $C_4$  alkyl;

the group  $NR^6OH$  wherein  $R^6$  is selected from hydrogen and alkyl, preferably  
 10 from hydrogen and  $C_1$  to  $C_4$  alkyl and most preferably hydrogen;

the group  $NR^7R^8$  wherein  $R^7$  and  $R^8$  are independently selected from hydrogen  
 and  $C_1$  to  $C_4$  alkyl.

The preferred group  $R^2$  is selected from the group consisting of hydrogen,  
 15 alkyl, haloalkyl, aryl, alkylaryl and aralkyl;

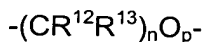
the group substituted alkyl, substituted haloalkyl, substituted acyl, substituted  
 aryl, substituted alkylaryl and substituted arylalkyl, wherein the substituent is  
 a group of formula



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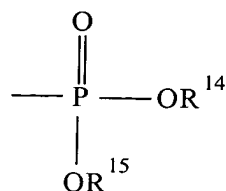
wherein  $R^{14}$  and  $R^{15}$  are independently selected from the group consisting of  
 hydrogen, halo, alkyl, aryl, alkanoyl, aralkyl, haloalkyl, haloaryl, haloalkyl aryl  
 and haloarylalkyl; and

25 the group wherein  $R^2$  is linked to  $R^1$  to provide the group  $-R^2-R^1-$  of formula



wherein  $n$  is 1 or 2,  $p$  is 0 or 1 and  $R^{12}$  and  $R^{13}$  are independently selected  
 from hydrogen, alkyl and haloalkyl.

More preferably  $R^2$  is selected from the group consisting of hydrogen  $C_1$  to  $C_8$  alkyl halo  $-(C_1 \text{ to } C_6)$  alkyl and  $C_1$  to  $C_6$  alkyl substituted by the group of formula



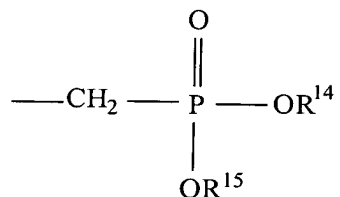
- 5 wherein  $R^{14}$  and  $R^{15}$  are independently selected from the group consisting of hydrogen and  $C_1$  to  $C_4$  alkyl; and

and the group wherein  $R^2$  is linked to  $R^1$  to provide the group  $-R^1-R^2-$  of formula



where  $R^{12}$  and  $R^{13}$  are independently selected from hydrogen,  $C_1$  to  $C_4$  alkyl and  $C_1$  to  $C_4$  haloalkyl.

- Even more preferred  $R^2$  is selected from the group consisting of hydrogen; and  
15  $C_1$  to  $C_4$  alkyl; the group of formula



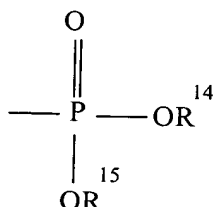
wherein  $R^{14}$  and  $R^{15}$  are independently selected from the group consisting of hydrogen and  $C_1$  to  $C_4$  alkyl; and the group wherein  $R^2$  is linked to  $R^1$  to provide the group  $-R^2-R^1-$  of formula



wherein  $R^{12}$  and  $R^{13}$  are selected from methyl and trifluoromethyl.

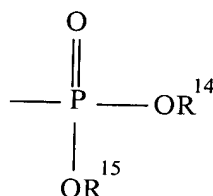
- Preferably the substituent  $R^3$  is selected from the group consisting of hydrogen, alkyl; haloalkyl; aryl; acyl; alkoxycarbonyl-substituted acyl; alkylaryl;  
25 aralkyl; and

the groups substituted alkyl, substituted haloalkyl, substituted acyl, substituted alkaryl and substituted aralkyl wherein the substituent is the group of formula



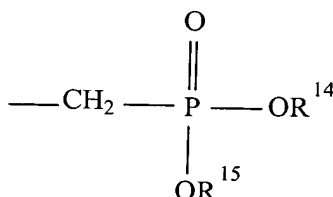
- 5 wherein R<sup>14</sup> and R<sup>15</sup> are independently selected from the group consisting of hydrogen, alkyl, aryl, aralkyl, alkylaryl, haloalkyl, haloaryl haloalkylaryl and haloaralkyl.

- 10 More preferably the substituent R<sup>3</sup> is selected from the group consisting of hydrogen, C<sub>1</sub> to C<sub>6</sub> alkyl, C<sub>1</sub> to C<sub>6</sub> alkanoyl, C<sub>1</sub> to C<sub>6</sub> haloalkyl and C<sub>1</sub> to C<sub>6</sub> alkyl and C<sub>1</sub> to C<sub>6</sub> alkyl substituted by the group of formula



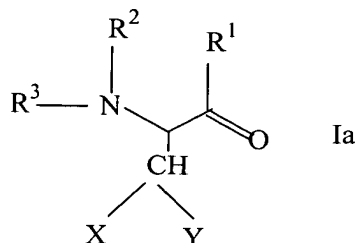
wherein R<sup>14</sup> and R<sup>15</sup> are independently selected from the group consisting of hydrogen and C<sub>1</sub> to C<sub>4</sub> alkyl.

- 15 Even more preferably the substituent R<sup>3</sup> is selected from the group consisting of hydrogen, C<sub>1</sub> to C<sub>6</sub> alkyl, C<sub>1</sub> to C<sub>6</sub> haloalkyl, C<sub>1</sub> to C<sub>4</sub> alkanoyl and the group of formula



- 20 wherein R<sup>14</sup> and R<sup>15</sup> are selected from the groups consisting of hydrogen and C<sub>1</sub> to C<sub>4</sub> alkyl.

In a particularly preferred embodiment the compounds of the invention are of formula Ia

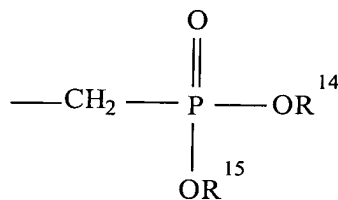


wherein  $\text{R}^1$ ,  $\text{R}^2$  and  $\text{R}^3$  are as hereinbefore defined and X and Y are independently selected from the group consisting of hydrogen, thiol, alkyl, haloalkyl, aryl, acyl, aralkyl, heterocyclic and heterocyclic alkyl.

The preferred groups X and Y are independently selected from hydrogen,  $\text{C}_1$  to  $\text{C}_4$  alkyl, aryl, aralkyl and heterocyclic.

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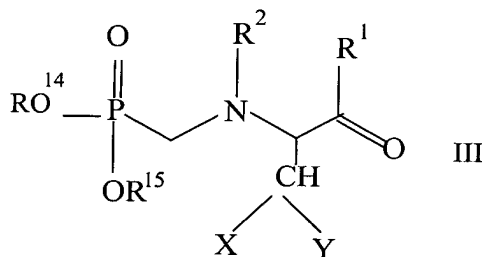
We have found that compounds of formula Ia are particularly insecticidally active where at least one of  $\text{R}^2$  and  $\text{R}^3$  is a group of formula



wherein  $\text{R}^{14}$  and  $\text{R}^{15}$  are as hereinbefore defined.

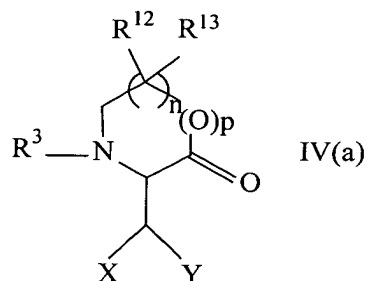
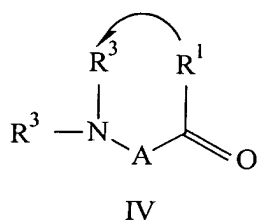
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Specific examples of such compounds include compounds of formula III



In one embodiment of the compounds of formula I the groups  $\text{R}^1$  and  $\text{R}^2$  are linked together to form a diradical linking group  $-\text{R}^2-\text{R}^1-$ . Such compound preferably have the formula IV and preferred examples of such compounds are of formula IVa

20



hereinbefore defined.

- When groups in formula I such as X and Y include heterocyclic;
- 5 examples of heterocyclic include 5 and 6 membered rings containing one or two heteroatoms selected from nitrogen, sulphur oxygen wherein the heteroring is optionally fused with a benzene ring. Specific examples include triazenyl, thiazolyl pyrrolyl imidazolyl, pyrazolyl, indolyl, isoindolyl, indazolyl, indoliny, isoindoliny, piperidiny, piperazeny, pyridyl, pyraziny.

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More preferred heterocyclic are indolyl and imidazolyl, most preferably 3-indolyl and 1-H-imidazol-4-yl.

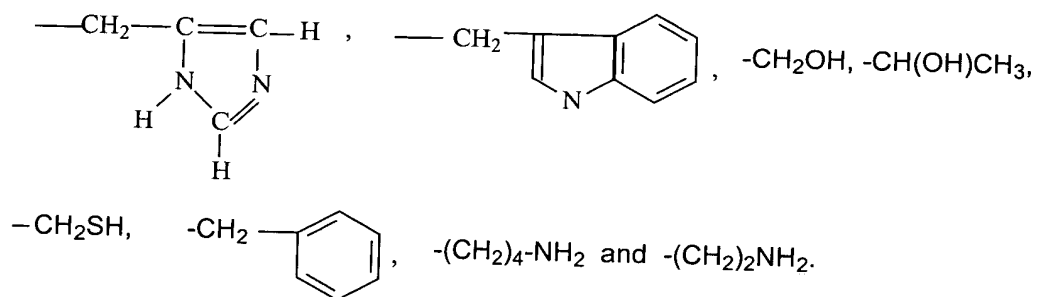
- When groups in formula I are, or include alkyl the preferred alkyl is of 1 to 6 carbon atoms and more preferably 1 to 4 carbon atoms.

- When groups in formula 1 such as R¹, R², R³, R⁵, X and Y are substituted groups, such as substituted alkyl, preferred substituents include hydroxy, amino, thio, C₁ to C₄ alkoxy, C₁ to C₄ alkylamino, aryl, hydroxyphenyl, halo, haloalkoxy and 5 and 6 membered heterocyclic rings containing one or two heterocarbons wherein the hetero ring is optionally fused with benzene.

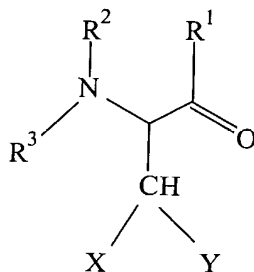
- When groups in formula I are or include aryl preferred aryl is phenyl.
- 25 When groups in formula I are or include acyl preferred acyl is selected from C₁ to C₆ alkyl carbonyl and benzoyl.



The group HC(X)(Y) in the preferred embodiment is derived from naturally occurring amino acids and accordingly is selected from the group consisting of -CH<sub>3</sub>, -CH(CH<sub>3</sub>)<sub>2</sub>, -CH<sub>2</sub>CH<sub>2</sub>SCH<sub>3</sub>, -CH<sub>2</sub>CH(CH<sub>3</sub>)<sub>2</sub>, -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>NHCNHNH<sub>2</sub>, -  
 5 CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>OH, -CH(CH<sub>3</sub>)CH<sub>2</sub>CH<sub>3</sub>,



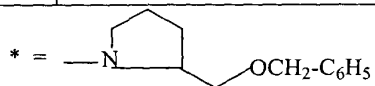
Specific examples of the compounds of formula Ia are shown in Table 1 below:



I a

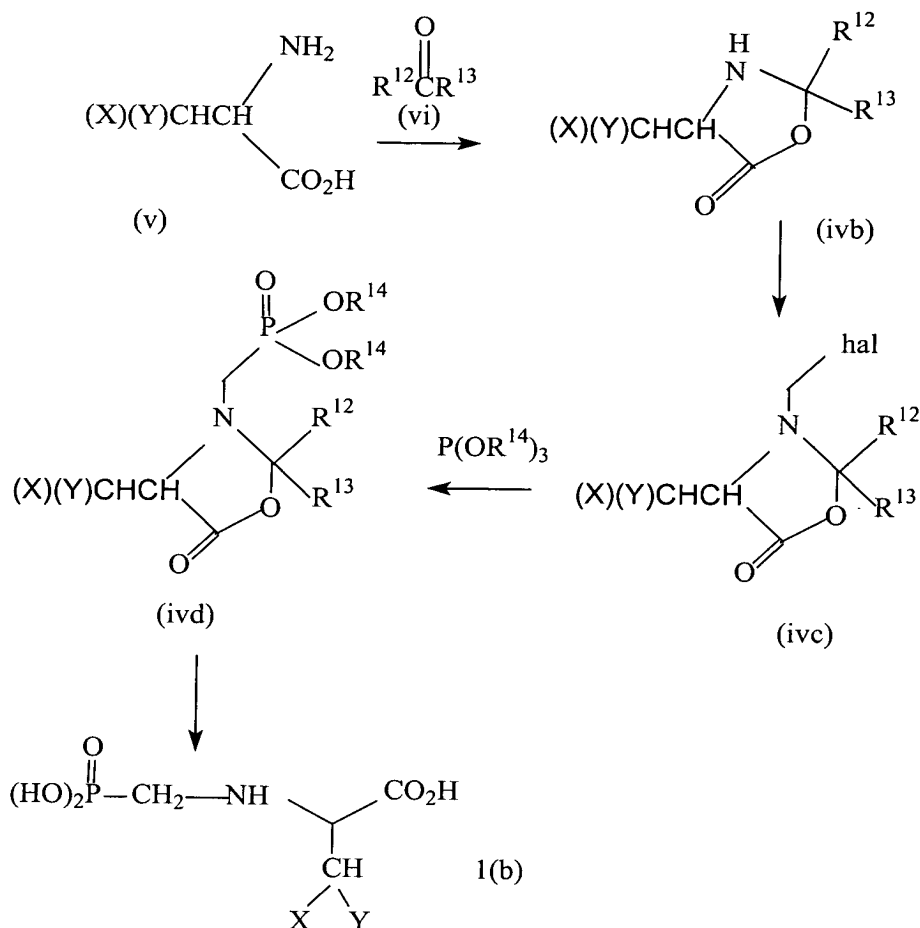
Table 1

	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	X, Y
1.	OH	H	CH <sub>2</sub> PO(OH) <sub>2</sub>	CH <sub>3</sub> , CH <sub>3</sub>
2.	NHOH	H	CH <sub>2</sub> PO(OH)(OCH <sub>3</sub> )	CH(CH <sub>3</sub> ) <sub>2</sub> , H
3.	NHOH	H	CH <sub>2</sub> PO(OH)(OCH <sub>3</sub> )	C <sub>6</sub> H <sub>5</sub> , H
4.	OH	H	CH <sub>3</sub>	H, H
5.	OH	H	CH <sub>2</sub> PO(OH) <sub>2</sub>	C <sub>6</sub> H <sub>5</sub> , H
6.	NHOH	H	CH <sub>3</sub>	H, H
7.	NHOH	H	CH <sub>2</sub> PO(OH)(OCH <sub>3</sub> )	H, H
8.		-OC(CF <sub>3</sub> ) <sub>2</sub> -	CH <sub>2</sub> PO(OCH <sub>3</sub> ) <sub>2</sub>	-CH(CH <sub>3</sub> ) <sub>2</sub> , H
9.	NHOH	H	CH <sub>3</sub> CO-	CH <sub>3</sub> , OH
10.	OCH <sub>3</sub>	H	CH <sub>2</sub> PO(OCH <sub>3</sub> ) <sub>2</sub>	C <sub>6</sub> H <sub>5</sub> , H
11.		-OC(CF <sub>3</sub> ) <sub>2</sub> -	BrCH <sub>2</sub> -	C <sub>6</sub> H <sub>5</sub> , H
12.	OCH <sub>3</sub>	CH <sub>2</sub> PO(OCH <sub>3</sub> ) <sub>2</sub>	CH <sub>2</sub> PO(OCH <sub>3</sub> ) <sub>2</sub>	CH <sub>3</sub> , CH <sub>3</sub>
13.		-OC(CF <sub>3</sub> ) <sub>2</sub> -	CH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub> , H
14.	NHOH	H	CH <sub>2</sub> PO(OH) <sub>2</sub>	CH <sub>3</sub> , CH <sub>3</sub>
15.	OH	H	CH <sub>3</sub>	CH <sub>3</sub> , CH <sub>2</sub> CH <sub>3</sub>
16.	NHOH	H	CH <sub>2</sub> PO(OH) <sub>2</sub>	H, CH(CH <sub>3</sub> ) <sub>2</sub>
17.	*	H	H	CH <sub>3</sub> , CH <sub>3</sub>
18.	OH	H	CH <sub>2</sub> PO(OCH <sub>3</sub> ) <sub>2</sub>	CH <sub>3</sub> SCH <sub>2</sub> , H



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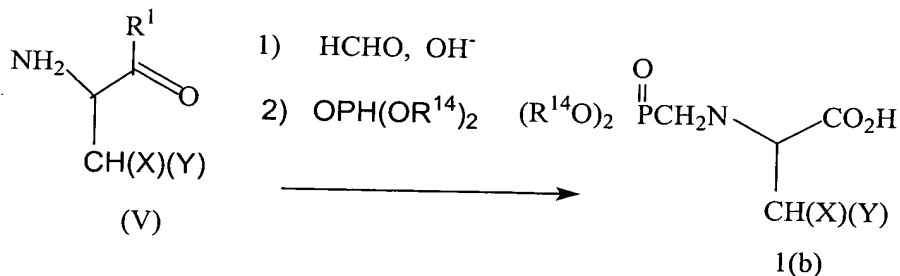
The insecticidal compounds of the invention may be prepared by a range of methods. In a preferred aspect the compounds of formula I and having specific formula ivb, ivc, ivd or ib are prepared according to scheme 1 below:

**Scheme 1**

Further compounds of formula 1 may be prepared from the compounds of  
 5 formula (ivb), (ivc), (ivd) and 1(b) by suitable methods.

In one aspect the preferred compounds are prepared by reaction of an amino  
 acid of formula (v) with a ketone of formula (vi) to provide a compound of  
 formula (ivb); reaction of the compound of formula (ivb) with paraformaldehyde  
 10 in the presence of a halogen particularly bromine to provide a compound of  
 formula (ivc) wherein  $hal$  is halogen (preferably bromine); reacting the  
 compound of formula (ivc) with a phosphite to provide a phosphonate ester of  
 formula (ivd) and hydrolysis, preferably in aqueous acid, to provide the  
 compound of formula 1(b).

In an alternative method the compounds of the invention are prepared by Mannich reaction as shown in Scheme 2:



**Scheme 2**

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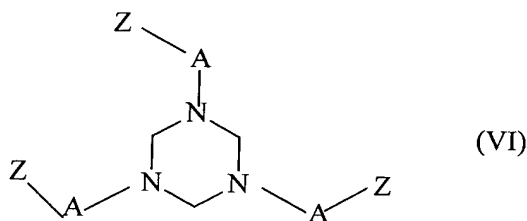
In this method an amino acid (formula V) is reacted with formaldehyde generally in an aqueous metal hydroxide medium. The reaction is preferably carried out with the reactants in approximately equimolar quantities and temperatures in the range of from  $-5^\circ\text{C}$  to  $15^\circ\text{C}$  are preferred.

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Phosphonomethylation is carried out by addition to the reacting mixture of a lower alkyl phosphite preferably dimethyl phosphite or diethyl phosphite. The phosphite is preferably approximately equimolar with respect to the amino acid. The reaction may be heated to a temperature in the range of from  $50^\circ\text{C}$  to  $100^\circ\text{C}$  to form the N-phosphonomethylated amino acid as the (formula 1b where  $\text{R}^{14}$  is lower alkyl) diethyl or monoethyl ester. The ester may optionally be hydrolysed in mineral acid such hydrochloric, sulphuric or phosphonic acid to provide the N-phosphonomethylamino acid (formula 1(b) wherein  $\text{R}^{14}$  is H).

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20 In a particularly preferred method methyl phosphonate or methyl phosphate ester compounds of the invention are prepared from a hexahydrazine of formula (VI):

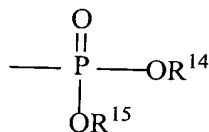


25 wherein Z is  $-\text{C}\equiv\text{N}$  or  $-\text{C}-\text{OOR}^5$ ;

wherein  $R^1$  is  $-C\equiv N$  or  $-COOR^5$ ;

wherein  $R^5$  is as hereinbefore defined but is typically other than hydrogen and preferably is  $C_1$  to  $C_6$  alkyl or halogenated  $C_1$  to  $C_4$  alkyl.

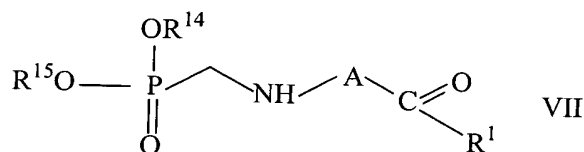
- 5 The compounds of formula I wherein one of  $R^2$  and  $R^3$  is:



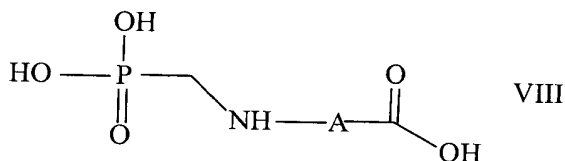
may be prepared by reaction of the hexahydrazine of formula VI with a phosphite of formula



- 10 to provide the product of formula:



The acid of formula

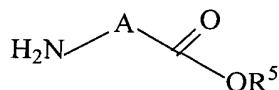


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may be prepared by hydrolyses of the compound of formula VII for example in a mineral acid.

The hexahydrotriazene may be prepared by reaction of the protected amino acid of formula

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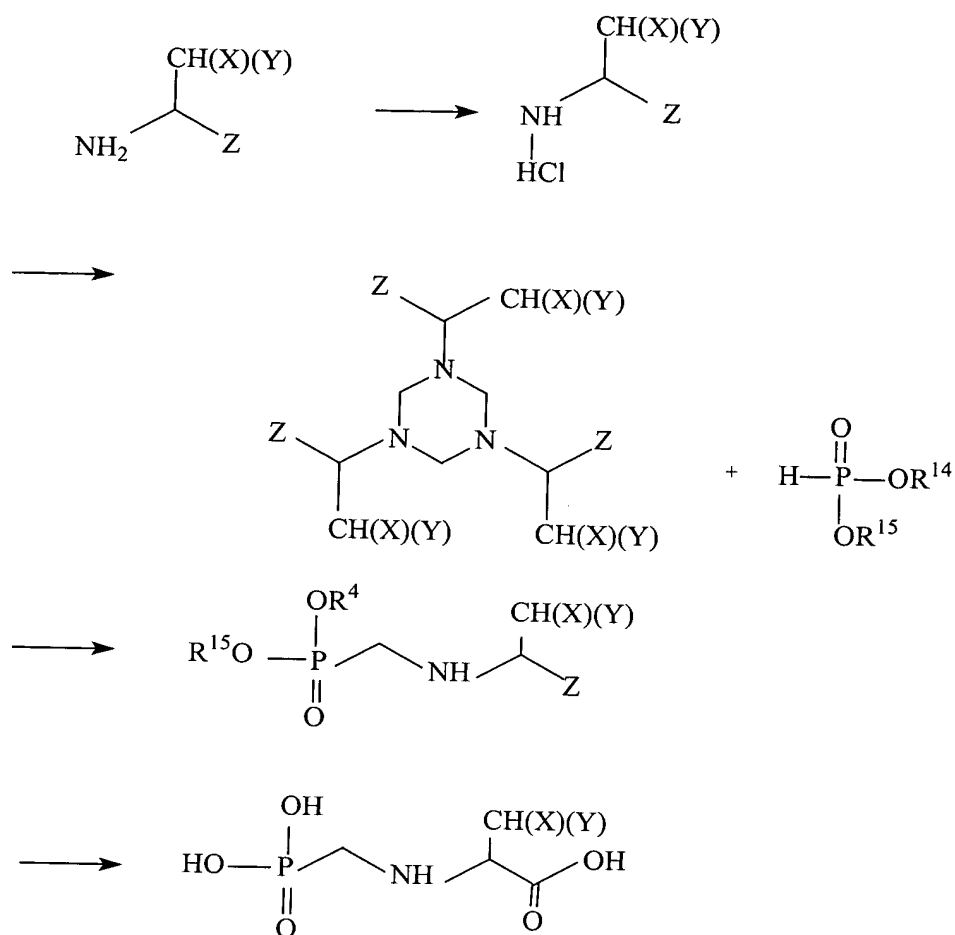


preferably as the hydrochloride salt with formaldehyde.

A preferred full scheme for this embodiment may be represented in Scheme 3

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below:



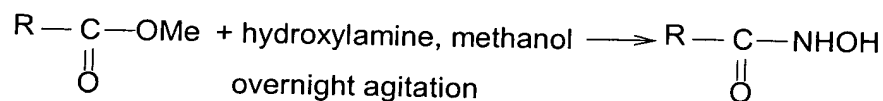
wherein Z is selected from  $-\text{COOR}^5$  and  $-\text{CN}$ .

### Scheme 3

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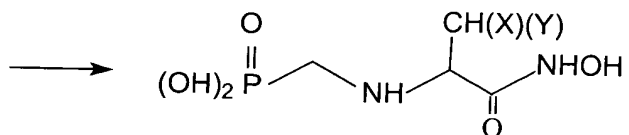
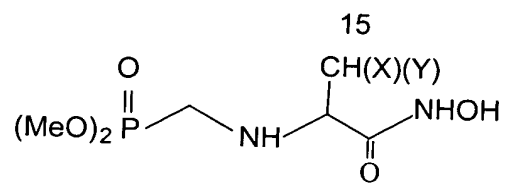
Further reactions which may be used to prepare the compounds of Table 1 and similar compounds including the following:

- 1) Preparation of hydroxamic acid derivatives may be prepared from acid derivatives such as lower alkyl esters by reaction with hydroxylamine

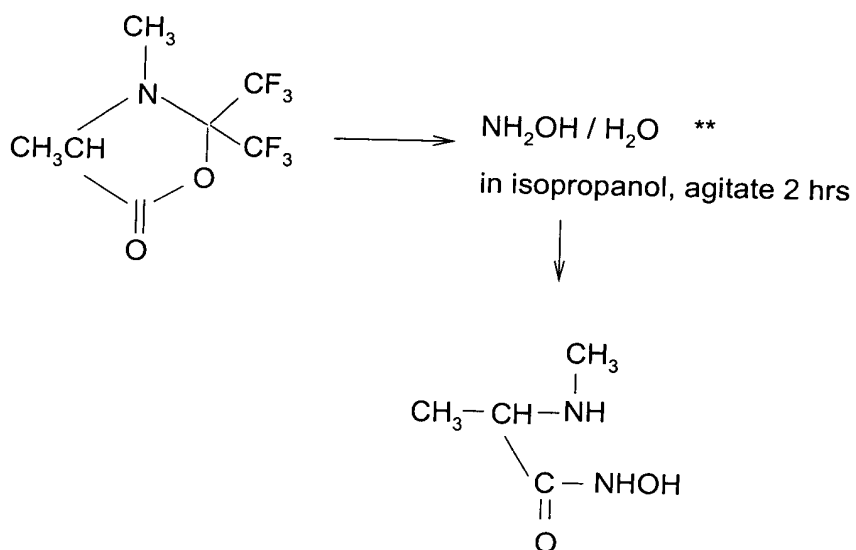


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- 2) Generation of a phosphonic acid from phosphonic acid dialkyl ester such as the dimethyl ester may be carried out by reaction with trialkyl silyl bromide in a solvent such as acetonitrile

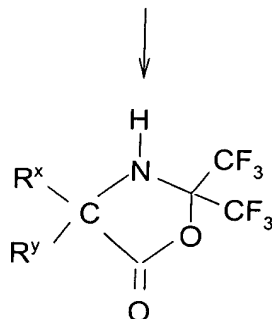
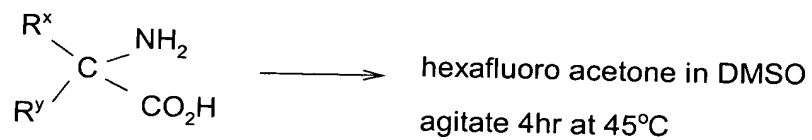


3) Ring-opening

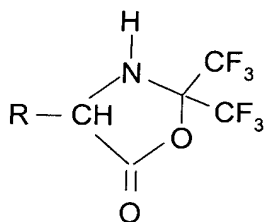


\*\*  $\text{NH}_2\text{OH} / \text{H}_2\text{O}$  formed by adding sodium bicarbonate to hydroxylamine hydrochloride and water

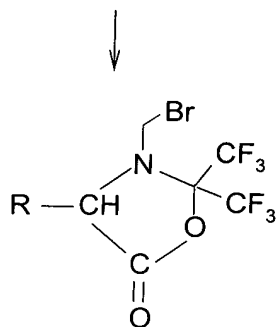
## 4) Ring-formation



## 5) Bromomethylation

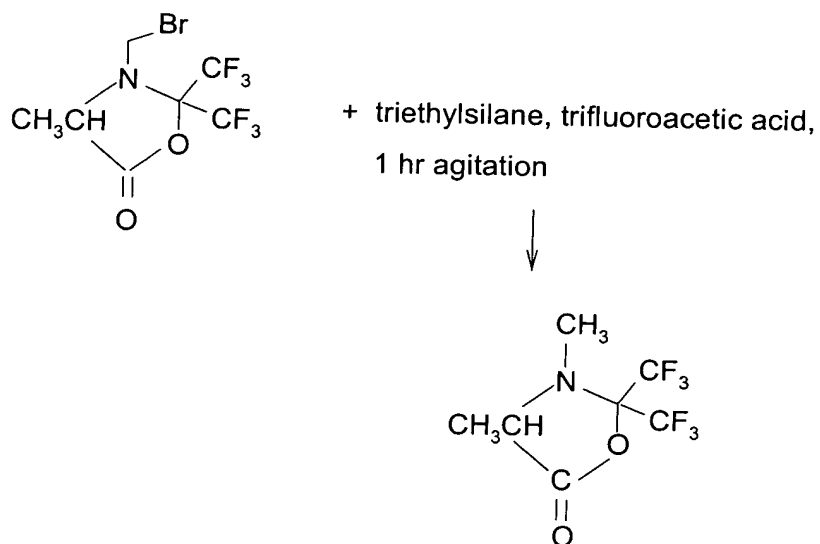


+ paraformaldehyde in phosphorous  
tribromide, 60°C, 2 hr agitation

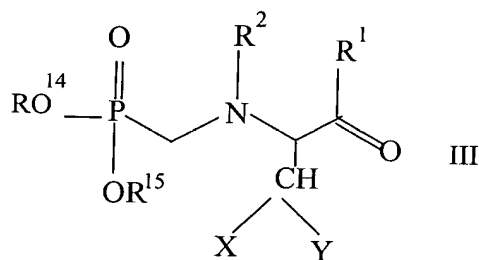


## 5 6) De-bromination



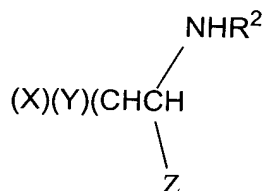


In one aspect the invention provides a method for the preparation of an insecticide of formula III



5

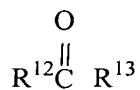
comprising reacting an amino acid or derivative thereof of formula (V)



wherein Z is  $-\text{CN}$  or  $\text{COOR}^5$

- 10 wherein  $\text{R}^5$  is selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclic and substituted heterocyclic;

with a compound for formula



wherein  $R^{12}$  and  $R^{13}$  are independently selected from hydrogen, halogen, alkyl and haloalkyl;

- 5 reacting the intermediate with a phosphite of formula  $HPO(OR^{14})(OR^{15})$  wherein  $R^{14}$  and  $R^{15}$  are independently selected from the group consisting of alkyl, to provide the compound of formula III and optionally hydrolysing the ester groups to provide a compound of formula III wherein  $R^{14}$  and  $R^{15}$  are hydrogen and  $R^1$  is hydroxy.

10

Preferred salts of compounds of formula I are salts formed with cations selected from the group consisting of alkali metals, alkaline earth metals, copper, zinc, manganese, nickel, ammonium, organic ammonium, organic sulphonium, and mixtures thereof. The most preferred salts are those in which

15 at least one of the groups  $R^5$ ,  $R^{14}$  and  $R^{15}$  is a counter ion and the others are hydrogen.

- Examples of organic ammonium may be selected from the group consisting of monoalkylammonium, dialkylammonium, trialkylammonium, monoalkenyl-
- 20 ammonium, dialkenylammonium, trialkenylammonium, monoalkanolammonium, dialkanolammonium, trialkenolammonium, heterocyclicammonium and aryl- ammonium. The preferred alkyl and alkenyl groups contain one to four carbon atoms.

- 25 The preferred salts are selected from the group consisting of alkali metals, alkaline earth metals, ammonium, alkyl ammonium (particularly isopropyl ammonium), trimesium and mixtures thereof.

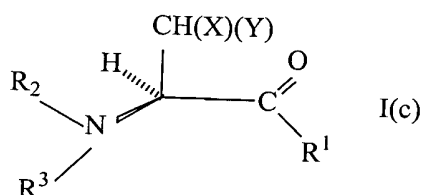
- Specific examples of the preferred compounds of the invention include:
- 30 sodium salt of N-phosphonomethylvaline, ammonium salt of N-phosphonomethylvaline, isopropylammonium salt of N-phosphonomethylvaline, trimesium salt of N-phosphonomethylvaline, N-phosphonomethylleucine, sodium salt of N-phosphonomethylleucine,

ammonium salt of N-phosphonomethylleucine, trimesium salt of N-phosphonomethylleucine.

5 The compounds of Formula Ia, III and IV include at least one chiral centre at the  $\alpha$  carbon atom (ie the carbon atom  $\alpha$  to the carboxyl or carboxylate group). The compounds of the invention may be in the form of the L-enantiomer the D-enantiomer or racemic mixtures thereof. In one embodiment the compound of Formula I is comprised of at least 80% of one enantiomer and preferably at least 90% of one enantiomer.

10

The compounds of the invention preferably have stereochemistry of formula I(c):



15 The insecticide of the invention will preferably include at least 60% of the compounds of formula I(a) having stereochemistry of formula I(c) and more preferably at least 80% and most preferably at least 90%.

20 Compositions may be prepared in a stereo selective manner from the naturally occurring L-series amino acids. Preferably the compound of the invention is prepared from an amino acid composition comprising at least 80% more preferably at least 90% by weight of the amino acids (on a molar basis) in L-form.

25 In a further embodiment the invention provides an insecticidal composition comprising one or more compounds of Formula I and an agriculturally acceptable carrier.

The insecticidally effective carrier may be any of the carriers known in the art and may provide a solid granular product, an aqueous solution or an emulsion containing the active component.

- 5    The compounds of formula I may be applied directly to insects or the locus of insects such as plants to be protected or soil.

The compounds of formula I may be used on their own to kill insects, inhibit the growth of insects or reduce the damage caused by insects but are  
10    preferably used in the form of a composition comprising a compound of the invention in admixture with a carrier comprising a solid or liquid diluent. Therefore, in yet a further aspect the invention provides an insecticidal compound as hereinbefore defined and carrier therefor.

- 15    The compositions of the present invention may be in the form of solids, liquids or pastes. The compositions include both dilute compositions which are ready for immediate use and concentrated compositions which may require dilution before use. Therefore, the concentration of the active ingredient in the compositions of the present invention will vary depending on the type of  
20    formulation and whether the composition is ready for use such as, for example, a dust formulation or an aqueous emulsion or whether the composition is a concentrate such as, for example, an emulsifying concentrate or a wettable powder, which is suitable for dilution before use. In general the compositions of the present invention comprise from 1 ppm to 99% by weight  
25    of active ingredient.

The solid compositions may be in the form of powders, dusts, pellets, grains, and granules wherein the active ingredient is mixed with a solid diluent. Powders and dusts may be prepared by mixing or grinding the active  
30    ingredient with a solid carrier to give a finely divided composition. Granules, grains and pellets may be prepared by bonding the active ingredient to a solid carrier, for example by coating or impregnating the preformed granular solid carrier with the active ingredient or by agglomeration techniques.

Examples of solid carriers include mineral earths and clays such as, for example, kaolin, bentonite, kiesulguhr, Fuller's earth, Attaclay, diatomaceous earth, loess, talc, chalk, dolomite, limestone, lime, calcium carbonate, powdered magnesia, magnesium oxide, magnesium sulfate, gypsum, calcium sulfate, prophyllite, silicic acid, silicates and silica gels; fertilizers such as, for example, ammonium sulfate, ammonium phosphate, ammonium nitrate and urea, natural products of vegetable origin such as, for example, grain meals and flours, bark meals, wood meals, nutshell meals and cellulosic powders; and synthetic polymeric materials such as, for example, ground or powdered plastics and resins.

Alternatively, the solid compositions may be in the form of water soluble or water dispersible dusts, powders, granules or grains wherein the active ingredient and the solid carrier are combined with one or more surface active agents which act as wetting, emulsifying and/or dispersing agents to facilitate the dispersion or solubilisation of the active ingredient in liquid.

Examples of surface active agents include those of the cationic, anionic and non-ionic type. Cationic surface active agents include quaternary ammonium compounds, for example, the long chain alkylammonium salts, such as cetyltrimethylammonium bromide. Anionic surface active agents include: soaps or the alkali metal, alkaline earth metal and ammonium salts of fatty acids; the alkali metal, alkaline earth metal and ammonium salts of ligninsulfonic acid; the alkali metal, alkaline earth metal and ammonium salts of arylsulfonic acids including the salts of naphthalenesulfonic acids such as butylnaphthalenesulfonic acid, and di- and tri-isopropylnaphthalenesulfonic acids, the salts of the condensation products of sulfonated naphthalene and naphthalene derivatives with phenol and formaldehyde, and the salts of alkylarylbenzenesulfonic acids such as dodecylbenzenesulfonic acid; the alkali metal, alkaline earth metal and ammonium salts of the long chain mono esters of sulfuric acid or alkylsulfates such as laurylsulfate and the monoesters of sulfuric acid with fatty alcohol glycol ethers. Nonionic surface active agents include: the condensation products of ethylene oxide with fatty alcohols such as oleyl alcohol and cetyl alcohol; the condensation products of ethylene oxide

with phenols and alkylphenols such as isooctylphenyl, octylphenol and nonylphenol; the condensation products of ethylene oxide with castor oil; alkyl polyglycoside surfactants; the partial esters derived from long chain fatty acids and hexitol anhydrides, for example sorbitan monolaurate, and their  
5 condensation products with ethylene oxide; ethylene oxide/propylene oxide block copolymers; lauryl alcohol polyglycol ether acetal; and lecithins.

The liquid compositions may comprise a solution or dispersion of the active ingredient in a liquid carrier optionally containing one or more surface active  
10 agents which act as wetting, emulsifying and/or dispersing agents. Examples of liquid carriers include: water, mineral oil fractions such as, for example, kerosene, solvent naphtha, petroleum, coal tar oils and aromatic hydrocarbons such as, for example, paraffin, cyclohexane, toluene, the xylenes, tetrahydronaphthalene and alkylated naphthalenes; alcohols such as, for  
15 example, methanol, ethanol, propanol, isopropanol, butanol, cyclohexanol and propylene glycol; ketones such as, for example, cyclohexanone and isophorone; and strongly polar organic solvents such as, for example, dimethylformamide, dimethylsulfoxide, N-methylpyrrolidone and sulfolane.

20 A preferred liquid composition comprises an aqueous suspension, dispersion or emulsion of the active ingredient which is suitable for application by spraying, atomising or watering. Such aqueous compositions are generally prepared by mixing concentrated compositions with water. Suitable concentrated compositions include emulsion concentrates, pastes, oil  
25 dispersions, aqueous suspensions and wettable powders. The concentrates are usually required to withstand storage to be capable of dilution with water to form aqueous preparations which remain homogenous for a sufficient time to enable them to be applied by conventional spray equipment. The concentrates conveniently contain from 20 to 80%, preferably 20 to 60% by  
30 weight of active ingredient.

Emulsion or emulsifiable concentrates are conveniently prepared by dissolving the active ingredient in an organic solvent containing one or more surface active agents. Pastes may be prepared by blending the finely divided active

ingredient with a finely divided solid carrier, one or more surface active agents and optionally an oil. Oil dispersions may be prepared by grinding together the active ingredient, a hydrocarbon oil, and one or more surface active agents. Aqueous suspension concentrates may conveniently be prepared by  
5 ball milling a mixture of the active ingredient, water, at least one surface active agent and preferably at least one suspending agent. Suitable suspending agents include: hydrophilic colloids such as, for example, poly(N-vinylpyrrolidone), sodium carboxymethylcellulose and the vegetable gums gum acacia and gum tragacanth; hydrated colloidal mineral silicates such as, for  
10 example, montmorillonite, beidellite, nontronite, hectorite, saponite, sauconite and bentonite; other cellulose derivatives; and poly(vinyl alcohol). Wettable powder concentrates may conveniently be prepared by blending together the active ingredient, one or more surface active agents, one or more solid carriers and optionally one or more suspending agents and grinding the mixture to give  
15 a powder having the required particle size.

The aqueous suspensions, dispersions or emulsions may be prepared from the concentrated compositions by mixing the concentrated compositions with water optionally containing surface active agents and/or oils.

20

Preferred solid compositions use water dispersible granule formulations comprising the active ingredient together with a solid carrier, optionally containing one or more solid or liquid surfactant active agents and other herbicidal adjuvants known to the art. The water dispersible granules may be  
25 prepared using methods known to the art, such as the wet granulation method.

The mode of application of the compositions of the invention will depend to a large extent on the type of composition used and the equipment available for its application. Solid compositions may be applied by dusting or any other  
30 suitable means for broadcasting or spreading the solid. Liquid compositions may be applied by spraying, atomising, watering, introduction into the irrigation water, or any other suitable means for broadcasting or spreading the liquid.

The compounds of the invention may be used in admixture with other insecticides to provide improved efficacy or more effective plant protection.

We have found that in combination with other insecticides provides a significant enhancement in activity which can be used to increase potency or to reduce the amount of other insecticide which is required to achieve pest control. While a wide range of known insecticides may be used in combination with the insecticide of the invention the composition of the invention preferably includes one or more insecticides selected from the group consisting of:

10

Organophosphorus compounds preferably selected from triazophos, monocrotophos, methamidophos, chlorpyrifos, parathion, acephate, profenofos, malathion, heptenophos;

15

Pyrethroids preferably selected from cypermethrin, cyhalothrin, lambdacyhalothrin, deltamethrin, fenvalerates, (alpha)-cypermethrin, cyfluthrin, fenpropathrin, etofenprox;

20

Carbamates preferably selected from aldicarb, bendiocarb, carbaryl, carbofuran, formetanates, pirimicarb;

25

Biopesticides preferably selected from bacillus thuringiensis, granuloses and nuclear polyhedrosis viruses, Beauveria bassiana, Beauveria brogniartii, baculoviruses, such as Autographa California, Spinosad;

Others selected from endosulfan, abamectin, XDE-105, diafenthiuron, fipronil, chlorfenapyr, tebufenocides, fenazaquin, imidaclopride, triazamates, fentin, amitraz, MK-242; and

30

4-Haloalkyl-3 heterocyclylpyridines and 4-haloalkyl-5-heterocyclylpyrimidines and their salts.

The insecticidal composition of the invention preferably includes compositions of the insecticide of formula I together with another insecticide wherein the



weight ratio is in the range of from 95:5 to 5:95 and more preferably from 9:1 to 1:9.

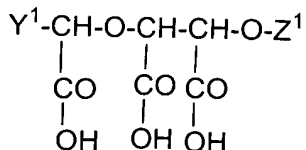
We have found that the activity of the insecticide of the invention may be significantly enhanced when it is used in combination with a chelating agent for divalent metals. Examples of chelating agents for divalent metals. Examples of chelating agents for divalent metals include compounds comprising a plurality of groups selected from carboxylic acid, carboxylate salt, hydroxyl amino, phosphoric acid, phosphonate salt.

Examples of preferred groups of chelating agents include amino polycarboxylic acid chelating agents, aromatic and aliphatic carboxylic acid chelating agents, amino acid chelating agents, ether polycarboxylic acid chelating agents, phosphonic acid chelating agents, hydroxycarboxylic acid chelating agents and dimethylglyoxime. The chelating agents may be in the form of the acid or salt particularly the sodium, potassium or ammonium salt.

Examples of aminopolycarboxylic chelating acids include ethylenediaminetetraacetic acid (EDTA), cyclohexanediaminetetraacetic acid (CDTA), cyclohexanediaminetetraacetic acid (CDTA), nitrilotriacetic acid (NTA), iminodiacetic acid (IDA), N-(2-hydroxyethyl)iminodiacetic acid (HIMDA), diethylenetriaminepentaacetic acid (DTPA), N-(2-hydroxyethyl)ethylenediaminetriacetic acid (EDTA-OH) and glycoletherdiaminetetracetic acid (GEDTA) ethylenediaminedisuccinic acid (EDDS) and salts thereof.

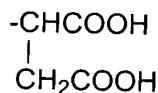
Examples of the aromatic or aliphatic carboxylic acid chelating agents to be used in the present invention include oxalic acid, succinic acid, pyruvic acid, salicylic acid and anthranilic acid, and salts, methyl esters and ethyl esters thereof. Further, examples of the amino acid chelating agents to be used in the present invention include glycine, serine, alanine, lysine, cystine, cysteine, ethionine, tyrosine and methionine, and salts and derivatives thereof.

Furthermore, examples of the ether polycarboxylic acid chelating agents to be used in the present invention include compounds represented by the following formula, compounds similar to the compounds represented by the following formula and salts (e.g., sodium salt) thereof:



5

wherein  $Y^1$  represents a hydrogen atom, a group represented by the formula:  $-\text{CH}_2\text{COOH}$  or a group represented by the formula:  $-\text{COOH}$ , and  $Z^1$  represents a hydrogen atom, a group represented by the formula:  $-\text{CH}_2\text{COOH}$  or a group represented by the formula



10

Examples of the hydroxy carboxylic acid chelating agents to be used in the present invention include malic acid, citric acid, glycolic acid, gluconic acid, heptonic acid, tartaric acid, lactic acid and salts thereof.

15 Examples of the electrolyte chelating agents of polymer (including oligomer) type to be used in the present invention include acrylic acid polymers, maleic anhydride polymers,  $\alpha$ -hydroxyacrylic acid polymers, itaconic acid polymers, copolymers comprising at least two of the constituting monomers of these polymers and epoxysuccinic acid polymers.

20

In addition, chelating agents to be used in the present invention further include ascorbic acid and thioglycolic acid, and salts thereof.

25 The most preferred chelating agents are amino polycarboxylic acids, aliphatic carboxylic acids and hydroxycarboxylic acids and the most preferred chelating agent is EDTA which may be used in the form of the sodium salt such as the tetrasodium salt or the other suitable salt particularly water soluble salts.

The invention further provides a method of controlling insects comprising applying to the insects or the locus of the insects an effective amount of the compound of Formula I.

- 5 The compounds of the invention are particularly effective in controlling insects in crops. Examples of pests on which the insecticide of the invention may be effective include: insect species of the orders Lepidoptera, Hemiptera, Orthoptera, Coleoptera, Psocoptera, Isoptera, Thysanoptera and Homoptera. These pests which cause massive losses to many horticultural and broadacre
- 10 crops and stored and manufactured grain products. Other examples of insect pests which may be controlled may include Diptera, Anaplura, Malophaga and Siponaptera cause parasitic infections in animals and man and Hymenoptera, Dictyoptera, Isoptera which are domestic and industrial pests.
- 15 Accordingly in a preferred embodiment of the method of the invention we provide a method of plant protection comprising applying to the plants an insecticidal composition as hereinbefore described.

The insecticides of the invention are particularly effective in controlling

20 Helicoverpa spp (Heliothis, cotton budworm) in cotton.

The invention will now be described with reference to the following examples. It is to be understood that the examples are provided by way of illustration of the invention and that they are in no way limiting to the scope of the invention.

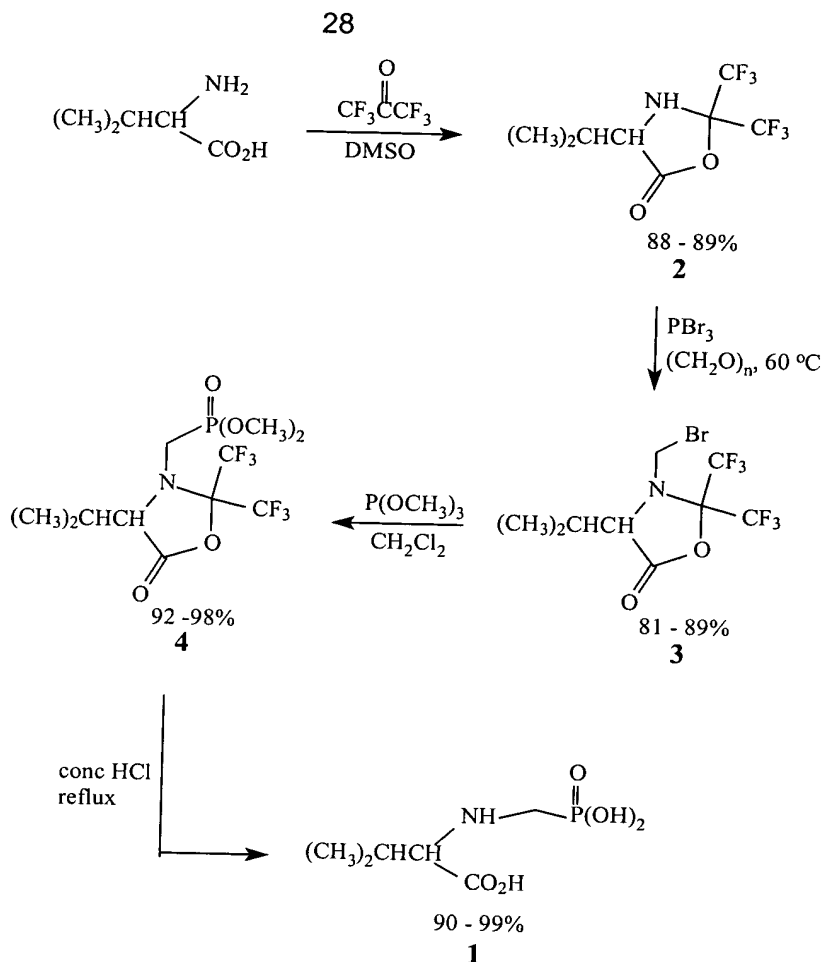
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### **Example 1**

#### **Preparation of N-Phosphonomethyl-L-Valine**

N-Phosphonomethyl-L-Valine (see compound designated C1 in table below) is believed to be a new composition of matter, and was prepared according to

30 Scheme 2 below.



**Scheme 1a. Synthesis of N-Phosphonomethyl-L-Valine**

Other amino acids may be used in a similar way to valine in the above scheme.

The specific details of reaction in the synthesis of D(+) N-Phosphonomethyl-L-Valine were as follows (see also general reaction scheme which is provided above).

**(a) Valine plus hexafluoroacetone**

Hexafluoroacetone (10g) was bubbled into a suspension of (L)-Valine (4.0g, 34.1mmol) in DMSO (30mL) in a 2-necked round-bottomed flask equipped with a dry-ice condensor. Slight warming was necessary to prevent the DMSO from freezing. After a clear solution was obtained,

excess hexafluoroacetone (2g) was bubbled into the reaction mixture, and stirring continued for 3-4h at  $\approx 45^{\circ}\text{C}$  (oil-bath temp). The excess hexafluoroacetone was distilled off into a water trap. The reaction mixture was poured into water (100mL) and extracted with  $\text{CH}_2\text{Cl}_2$  (2 x 50mL). The combined organic extracts were washed with water (2 x 50mL) and dried over anhydrous  $\text{Na}_2\text{SO}_4$ . The mixture was distilled at atmospheric pressure to remove the  $\text{CH}_2\text{Cl}_2$ .

Yield : 8.02g (89%) – clear colourless liquid.

#### 10 (b) Bromination

A mixture of valine trifluoromethyl oxazolidinone (8.0g, 30mmol), paraformaldehyde (1.81g) and phosphorus tribromide (6mL) was heated at  $60^{\circ}\text{C}$  (oil-bath temp) for 2h.

15 The reaction mixture was distilled under vacuum ( $\approx 0.1\text{mmHg}$ )

Fraction1,  $25\text{-}30^{\circ}\text{C}$  –  $\text{PBr}_3$

Fraction 2,  $40\text{-}50^{\circ}\text{C}$  – clear colorless liquid, 9.6g (89%)

#### (c) Phosphonate Ester Moiety

20 Trimethylphosphite (1.19mL, 10mmol, 1.2equiv) was added dropwise to a solution of valine-methylbromide (3.0g, 8.3mmol, 1equiv) and  $\text{CH}_2\text{Cl}_2$  (5mL) at room temp. Stirring was continued for 1h. The reaction mixture was concentrated in vacuo, white solid, 3g (92%).

#### 25 (d) Hydrolysis of Phosphonate Ester

A soln of the valine-methylphosphonate (2.0g, 5mmol) and concentrated  $\text{HCl}$  (6mL) was heated at reflux for 5h. The reaction mixture was concentrated in vacuo. The residue was dissolved in ethanol. Propylene oxide (2mL) was then added. A white solid precipitated. Ether (25mL) was then added, and stirring continued for 15min. The solid product was isolated by suction filtration, washed with ether and dried in vacuo. Yield 1.02g (93%) – white solid (semi-solid at room temp).

- (e) The L(-) isomer of N-phosphonomethylvaline may be prepared in the same manner as described above by using the D(+) enantiomer of valine.

5 (f) **Optical Activity of N-phosphonomethylvaline**

Relative optical rotation has been measured for the proposed L- and D-isomers of N-phosphonomethylvaline as well as their racemic mixture.

10 The optical rotation study was carried out on a ca. 0.25 M solutions of the above samples in the solvent comprised of distilled water (98% v/v),  $\text{KH}_2\text{PO}_4$  (1.68 g/L), methanol (2.0 % v/v) and 88 %  $\text{H}_3\text{PO}_4$  (0.2%). The following results were obtained.

1. The sample which was prepared from **L**-Valine (starting material) showed relative optical rotation ( $[\alpha]_D$ ) to be  $+7.7^\circ$ .  
 15 This was calculated according to the following relationship ( $[\alpha]_D = (100 \times \alpha / (1 \times C))$ )  
 where  $\alpha$  is the measured angle ( $^\circ$ ) ( $0.8^\circ$ )  
 $C$  is concentration of the sample (g/100ml) (5.2 g/100 ml)  
 $1$  is length of observation tube (dm) (2 dm)
- 20 2. The sample which was prepared from **D**-Valine (starting material) showed relative optical rotation ( $[\alpha]_D$ ) to be  $-12.5^\circ$ .  
 where  $\alpha$  is the measured angle ( $^\circ$ ) ( $-1.2^\circ$ )  
 $C$  is concentration of the sample (g/100ml) (4.8 g/100 ml)  
 $1$  is length of observation tube (dm) (2 dm)
- 25 3. The sample which was prepared from **DL**-Valine (racemic) (starting material) showed relative optical rotation ( $[\alpha]_D$ ) to be  $0^\circ$  (as expected).

**Examples 2 to 17**

30 The compounds of examples 2 to 17 were prepared by a method in accordance with Example 1 and in accordance with information provided for the compounds in Table 1. The reagents were modified in accordance with the general procedure of scheme 1. Compounds 1 to 17 were subjected to bioassay in accordance with the following procedure and the results are shown in Table 2.

### ***Helicoverpa* colony maintenance**

*H. armigera* were obtained from the CSIRO Entomology, Indooroopilly, QLD, Australia. *H. armigera* and *H. punctigera* were housed in independent constant temperature rooms (25-27°C) with a 16/8 hour light/dark cycle. Larvae were reared in individual cups containing 1.5cm cubes of media. Media comprised 234g Haricot beans, 14g agar, 35g Tortula yeast, 50g wheatgerm, 3.5g ascorbic acid, 1.1g sorbic acid and 2.2g p-hydroxybenzoic methylester made up to 1L with dH<sub>2</sub>O, and was supplemented with 200mg penicillin, 200mg streptomycin and 16mg prochloraz. For every third generation of larvae raised, 50mg chloramphenicol was added to 1L of media. Care was taken during the rearing process to limit to potential for the development of contamination. To maintain viability, new larvae obtained from the field were added to the colony every third to fourth generation.

### ***Media bioassay***

This assay was performed to investigate the efficacy of compounds in inhibiting larval growth. Media was prepared in an identical manner to that described above, and 5ml was added to wells containing 500µl of test compound. Each compound was tested at 1.25, 2.5, 5 and 10mM final concentration. The inhibitor was mixed evenly through the media, then the mixture was allowed to set. The media containing inhibitor was then divided between five plastic cups and two neonatal larvae were placed on the media in each cup. Larvae were left undisturbed for five days at 25-27°C in a room with a 16/8 hour light/dark cycle. Controls, containing the solvent dimethyl sulfoxide (DMSO) which was used for dissolving the inhibitor, were included in each assay. After 5 days all cups were transferred to -20°C and left overnight before removal and weighing of the larvae. Larval weights were compared between treated and control groups. The results were expressed as a % inhibition, I, calculated as follows:  $I = 100(1 - A)$ , where A is given by [(weight of control larvae) minus (weight of treated larvae)] divided by (weight of control larvae).

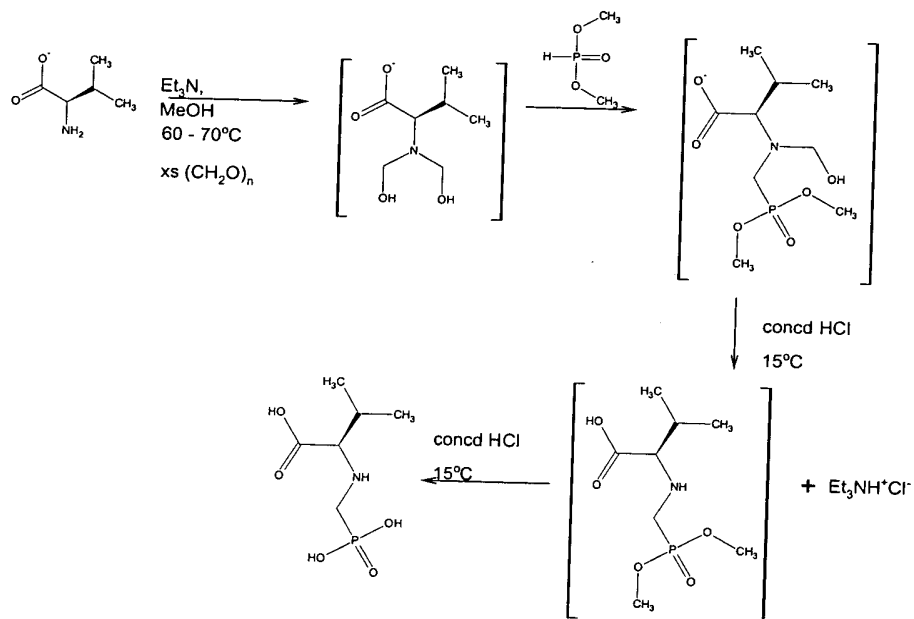
Table 2

Ex.	Simple Name	% inhibition, I	Systematic Name
C1	N-phosphonom ethyl valine	62.5	3-Methyl-2-(phosphonom ethyl-amino)-butyric acid
C2	leucine methylphosphonate hydroxamic acid	59.7	[(1-Hydroxycarbamoyl-3-methyl-butylamino)-methyl]-phosphonic acid monomethyl ester
C3	phenylalanine-N-methyl phosphonyl hydroxamic acid	49.9	[(1-Hydroxycarbamoyl-2-phenyl-ethylamino)-methyl]-phosphonic acid monomethyl ester
C4	N-methylalanine	49.1	2-Methylamino-propionic acid
C5	phenylalanine-N methyl phosphonic acid	45.0	3-Phenyl-2-(phosphonom ethyl-amino)-propionic acid
C6	N-methylalanine hydroxamic acid	43.9	N-Hydroxy-2-methylamino-propionamide
C7	alanine hydroxamic acid-N methylphosphonate half methyl ester	41.6	[(1-Hydroxycarbamoyl-ethylamino)-methyl]-phosphonic acid monomethyl ester
C8	leucine intermediate	35.2	4-(2-methylpropyl)-3-(dimethoxy-phosphonomethyl)-2,2-bis-trifluoromethyl-oxazolidin-5-one
C9	N-acetyl phenylalanine hydroxamic acid	34.7	2-Acetylamino-N-hydroxy-3-phenyl-propionamide
C10	threonine methyl phosphonate derivative	34.4	2-[(Dimethoxy-phosphorylmethyl)-amino]-3-hydroxy-butyric acid methyl ester
C11	phenylalanine methyl phosphonic acid intermediate	29.2	4-Benzyl-3-bromomethyl-2,2-bis-trifluoromethyl-oxazolidin-5-one
C12	valine N,N di-methyl phosphonate derivative	28.0	2-[Bis-(dimethoxy-phosphorylmethyl)-amino]-3-methyl-butyric acid methyl ester
C13	phenylalanine hydroxamate intermediate	26.7	4-Benzyl-3-methyl-2,2-bis-trifluoromethyl-oxazolidin-5-one
C14	valine N-methyl phosphonate hydroxamic acid	24.4	[(1-Hydroxycarbamoyl-2-methyl-propylamino)-methyl]-phosphonic acid
C15	N-methylisoleucine	24.4	3-Methyl-2-methylamino-pentanoic acid
C16	leucine methylphosphonic acid hydroxamate	24.3	[(1-Hydroxycarbamoyl-3-methyl-butylamino)-methyl]-phosphonic acid
C17	valine derivative	20.3	2-Amino-1-(2-benz yloxymethyl-pyrrolidin-1-yl)-3-methyl-butan-1-one



**Example 18**

N-Phosphonomethyl-L-valine may also be prepared from (L)-valine by Mannich reaction according to the method of Scheme 3 shown below. This method is particularly suitable for larger scale preparations.

**Scheme 3**

10 **Example 19. Control of *Helicoverpa* spp. larvae in a commercial cotton crop.**

A field trial was conducted in a commercial cotton-growing region of Western Australia, as outlined below.

**Location:** Kununurra, Western Australia.

**Dominant pest species:** *Helicoverpa armigera*: 186 (81%) of 230 third instar were *H. armigera*

**Crop:** Cotton cv Delta Pine Emerald (broad leaf type).

**Planting Details:** 7 to 8 plants per m of row, 2 rows 90 cm apart on beds at 1.8 m centres .

**Plant Details:** About 1 metre tall at application. High foliage density;

**Crop Stage:** Mid flowering.

**Phytotoxicity at 7 days**

**after application (DAA):** None.

The trial was laid out as a randomized complete block experiment; with four blocks each containing one plot of each insecticidal treatment and one plot of the untreated control. Each block was comprised of consecutive plots 10 m long within the same strip of cotton. Buffer zones of several metres were left untreated between plots.

Treatments were:

C1 @ 2.0kg/ha

EDTA (previously been shown to have the ability to influence larval survival) @2.0 kg/ha and

C1 plus EDTA (1.0 kg/ha each).

No rain fell during the period of the trial, however dews formed before sunrise each day. Leaves were also coated with dust and ash from local bush fires.

At 3 days after application (3DAA) total numbers of live viable *Helicoverpa* spp. larvae (TLVA) were counted on 10 terminals per plot.

Results were as follows.

**Table 19.1. Influence of C1 and EDTA on the population of *Helicoverpa* spp.**

Treatment		Mean number TLVA*/ 10 Terminals	
C1 (kg/ha)	EDTA (kg/ha)	-1DAA	3DAA
2	0	0.0	3.9
0	2	0.0	6.0
1	1	0.0	3.2
0	0	0.1	5.4

Although EDTA alone had no apparent influence on larval survival in this experiment (possibly because of washing by the dew or leaf contamination),

C1 reduced the larval numbers by over 25% and the combined treatment of C1/EDTA at the same payload/ha reduced larval numbers by over 40%.

5 The trial showed that C1 plus EDTA was effective against *Helicoverpa* spp. infesting cotton and that mixing C1 and EDTA was more effective than using the components alone.

**Example 20: Insecticidal activity of racemic N-phosphonomethyl valine (C1) compared with its D and L isomers.**

10

The development of *Helicoverpa* larvae on geranium plants was assessed in a glasshouse. Commercially grown geranium seedlings were potted (one plant/pot) two weeks prior to use. Seedlings used for experimental purposes were about 150mm tall, with 4-7 leaves. On the day of treatment, plants were ranked by size and the ranking divided by the treatment number. Within these groupings plants were randomly allocated to a treatment grouping to provide 7 pots (plants) per treatment. Each group was isolated and sprayed with insecticidal treatments or water using a hand operated misting sprayer. Plants were then allowed to dry for approximately 1-2 hours before being placed in insect-proof cages in the glasshouse (one treatment/cage). Neonatal larvae of *H. armigera* were grown as outlined previously and 20 first instar larvae applied by evenly distributing them across all the leaves of each plant (generally 5 or 6 leaves) using a fine paint brush.

25 Assessments the total number of live, viable and active (TLVA) larvae, together with a subjective assessment of the percentage damage to leaves of each plant on days 3, 5 and 7 after application.

30 Two trials were conducted; one with just the isomeric variants of N-phosphonomethyl valine (C1) applied to the test plants and the second using two additives that had previously been found to improve the insecticidal activity of C1. These additives were EDTA (disodium, Sigma) and endosulfan (Endosulfan 350EC, Nufarm Ltd, 350g/L endosulfan). In this trial EDTA was

used at the same molar concentration as the racemic or isomeric C1. An appropriate sub-lethal concentration of endosulfan (suitable for use in glasshouse evaluations) was determined in previous dose-response evaluations. The suitable dose rate was  $1/250^{\text{th}}$  of the rate recommended for use in the field (label rate, 2100mL/Ha).

Isomeric versions of C1 were produced by the method outlined in Example 18, commencing with valine of known optical rotation properties.

The treatments are shown in Table 20.1.

**Table 20.1. Products and dose rates used in evaluation of the isomeric forms C1.**

<i><b>Trial 1.</b></i>	
<b>Code</b>	<b>Product and Dose</b>
C1	C1 manufactured from D,L-valine, designated 'racemic mixture' 25mM dose
L – C1	C1 manufactured using L-valine to provide the D(+) isomer 25mM dose
D – C1	C1 manufactured using D–valine, to provide the L(-) isomer 25mM dose
UTC	Untreated Control (sprayed with dilution water)

15

<i><b>Trial 2.</b></i>	
<b>Code</b>	<b>Product and Dose</b>
C1 mix	C1 (25mM) plus EDTA (25mM) plus endosulfan ( $1/250^{\text{th}}$ label rate)
L - C1 mix	L - C1 (25mM) plus EDTA (25mM) plus endosulfan ( $1/250^{\text{th}}$ label rate)
D - C1 mix	D - C1 (25mM) plus EDTA (25mM) plus endosulfan ( $1/250^{\text{th}}$ label rate)
UTC	Untreated Control (sprayed with dilution water)

At -0.5, 3, 5 and 7DAA, numbers of *Helicoverpa armigera* larvae per leaf and per plant were counted, as well as a subjective (visual) assessment made of the percent leaf damage per plant.

- 5 Influence of the treatments on development of the population of *Helicoverpa spp.* and leaf damage produced by the larvae to 7 days after application (DAA) in the two trials are illustrated in Table 20.

10 **Table 20.2. Insecticidal efficacy of racemic and isomeric forms of N-phosphonomethyl valine (C1) in glasshouse assessments.**

<i>Trial 1</i>		
<u>Treatment</u>	Mean number of larvae/leaf at 7DAA	Estimated leaf damage (%) at 7DAA
C1	2.8	43
L - C1	2.3	35
D - C1	3.5	55
UTC	3.6	63

<i>Trial 2</i>		
<u>Treatment</u>	Mean number of larvae/leaf at 7DAA	Estimated leaf damage (%) at 7DAA
C1 mix	1.5	28
L - C1 mix	0.6	22
D - C1 mix	2.4	55
UTC	3.2	70

- 15 Insecticidal activity appeared to reside primarily with C1 manufactured using the L isomer of valine. This version of the compound remained compatible with EDTA and endosulfan.

**Example 21: Compatibility of C1/EDTA with other insecticides.**

- 20 (a) Endosulfan. Field trial on cotton.

Trial 2 in Example 20 indicated compatibility of endosulfan with a C1/EDTA mixture in the glasshouse. This was confirmed in a field trial on cotton conducted under the same conditions as those outlined for Example 19. This trial was however conducted later in the growing season with plants in the late

flowering stage. Plants in this trial had clean leaves and neither rain nor dews were recorded over the trial period. Results are illustrated in Table 21.1.

5 **Table 21.1 Compatibility of Endosulfan with a C1/EDTA mix in the field**

Treatment		TLVA* / 10 terminals	
C1 plus EDTA (1Kg/ha of each)	Endosulfan* (mL/ha)	-0.5DAA	Mean 3-7DAA
-	2100	1.6	1.9
-	210	1.5	4.1
+	210	1.6	1.6
-	0	1.3	3.9

\* Endosulfan 350EC, Nufarm. Label (recommended field) rate for treatment of helicoverpa in cotton is 2.1L/Ha.

10 Results confirmed compatibility of the C1/EDTA mix with endosulfan. Similar larval kill was obtained with C1/EDTA (1Kg/Ha each) supplemented with endosulfan at 1/10<sup>th</sup> label rate as was obtained with endosulfan at full label rate.

15 **Example 21cont: Compatibility of C1/EDTA with other insecticides.**

(b) Spinosad. Field trial on cotton

20 A field trial was conducted in a commercial cotton-growing region of southern QLD (Dalby, Darling Downs). Pre-flowering cotton plants (7 to 8 plants/metre of row, two rows 90cm apart on beds at 1.8m centres. The trial was laid out as a complete block experiment; with four blocks each containing one plot of each insecticide treatment and one plot of the untreated control. Each block was six rows wide by 15m long, with the central 4m by 10 m sprayed. The treatments are tabulated below:

25

Products and dose rates used in the evaluation of the compatibility of spinosad with the C1/EDTA mixture were:

1. C1 (1Kg/Ha) plus EDTA (disodium (1Kg/Ha).
2. Spinosad (Tracer, Dow Elanco, at label rate for treatment of

helicopter in cotton; 150 mL/Ha)

3. Spinosad, 15 mL/Ha (1/10<sup>th</sup> label rate)
4. C1 (1Kg/Ha) plus EDTA (disodium (1Kg/Ha) plus Tracer (Spinosad) 15 mL/ha.
5. Untreated Control

At -0.5, 3 and 8DAA, *Helicoverpa* spp. larvae, damaged squares and bolls were evaluated on a per metre of row basis. Rain (5mm) fell during day 7 after treatment. Influence of the treatments on development of the population of *Helicoverpa* spp. over the trial period is illustrated in Table 21.2

5

**Table 21.2. Population of *Helicoverpa* spp. over the trial period.**

Treatment				Mean number TLVA*/ metre of row			Damaged squares and bolls/ metre of row
Code	C1 kg/ha	EDTA Kg/Ha	Tracer mL/Ha	0.5DAA**	3DAA	8DAA	8DAA
1	0	0	0	2.25 b	2.25 c	4.63 b	3.13 d
2	1	1	0	1.50 ab	0.88 b	2.63 a	1.50 c
3	0	0	150	1.75 b	0.38 a	1.88 a	0.75 a
4	0	0	15	1.50 ab	0.88 ab	3.00 a	1.38 bc
5	1	1	15	1.50 ab	0.75 ab	2.00 a	0.88 ab
LSD 95%				1.46	0.73	1.37	0.57

As in the previous examples, the reductions in larval numbers obtained when the individual components of mixed treatments were applied to cotton were too large to facilitate the demonstration of synergy. As demonstrated in the previous examples with endosulfan however, additive benefits were obtained by combining the C1/EDTA mixture with a spinosad. As with endosulfan, reductions in insect number were similar when the commercial insecticide was used at full label rate as when it was used at 1/10<sup>th</sup> the recommended rate with the C1/EDTA mix.

10

15

**Example 21cont: Compatibility of C1/EDTA with other insecticides.**

(c) Chlorpyrifos. Field trial on peas.

- 5 A field trial was conducted as a single large plot trial in commercial pidgeon pea crop located in northern NSW (Dubbo). (7 to 8 plants/metre of row, six rows, 20m long). Each sampling site consisted of one metre of row, well separated from surrounding treatments. Each treatment was randomly replicated four times across the plot. Insect populations were assessed by the
- 10 'beat sheet' method, as visual assessment of larvae in standing crops of this type is difficult. The beat sheet method of larval assessment consists of placing a white sheet under the section of crop to be assessed and the crop is vigorously shaken to dislodge larvae onto the sheet. The treatments are tabulated below:
- 15
1. C1 (1Kg/Ha) plus EDTA (disodium (1Kg/Ha).
  2. Chlorpyrifos (Pirate 300g/L EC, Nufarm, at label rate for treatment of helioverpa in cotton; 4.0L/ha)
  3. Chlorpyrifos 0.4L/ha (1/10<sup>th</sup> label rate)
  4. C1 (1Kg/Ha) plus EDTA (disodium (1Kg/Ha) plus Pirate 0.4L/ha.
- 20
5. Untreated Control

Pre-treatment and at 2 and 5DAA, the number and *Helicoverpa* spp. larvae were evaluated on a per metre of row basis.

25 **RESULTS**

Influence of the treatments on development of the population of *Helicoverpa* spp. over the trial period is illustrated in Table 21.3.



**Table 21.3. Insecticidal activity of chlorpyrifos combinations.**

Code	Mean number of small larvae / metre of row at 5DAA	Mean number of medium larvae / metre of row at 5DAA	Mean number of large larvae / metre of row at 5DAA	Mean total number of larvae / metre of row at 5DAA
1	0.3	5.0	6	11.3
2	0.0	2.3	3.8	6.0
3	1.5	6.0	4.8	12.3
4	0.0	2.5	3.8	6.3
5	1.5	7.8	5.8	15.0

The sum of the reductions in total larvae/metre of row obtained when the C1/EDTA component and the '1/10<sup>th</sup> rate' chlorpyrifos treatment were used alone was less than the larval reduction noted when the two treatments were used together. This indicates synergistic insect control by the combined treatment. The results of this trial were consistent with previous trials in the glasshouse, which indicated that medium and large larvae were little affected by exposure to the C1/EDTA mixture alone. The results of this trial demonstrate that medium and large larvae are well controlled by a C1/EDTA when combined with a low rate chlorpyrifos.

**Example 21cont: Compatibility of C1/EDTA with other insecticides.**

(d) Abamectin. Glasshouse trial. *Helicoverpa armigera* on geranium seedlings

The potential of abamectin as a co-insecticide with a mixture of C1plus EDTA was assessed by exposing *Helicoverpa armigera* larvae to the mixture and its component parts in a glasshouse experiment. Geranium seedlings were prepared and treated as outlined in Example 20, except that the plants were sprayed with products outlined below.

1. Abamectin 18g/L EC (Nufarm, trial formulation) applied at 1/250<sup>th</sup> the recommended rate for field use (6mL/L). A previous dose titration had indicated that this dilution was likely to give a sub-lethal response.
2. C1 (25mM) plus abamectin (1/250<sup>th</sup> of 6mL/L).

3. C1 (25mM) plus EDTA (disodium, 25mM) plus abamectin (1/250<sup>th</sup> of 6mL/L).
  4. Untreated Control
- 5 Assessments the total number of live, viable and active (TLVA) larvae, together with a subjective assessment of the percentage damage to leaves of each plant were made on days 3, 5 and 7 after application.

The number of *Helicoverpa armigera* larvae per leaf, as well as a subjective (visual) assessment of the percent leaf damage per plant was made on day 7 after application (7DAA).

### RESULTS

Influence of the treatments on survival of *H. armigera*. is illustrated in Table 21.4.

**Table 21.4. Insecticidal activity of abamectin combinations.**

Code	Mean number of larvae / leaf at 7DAA	Estimated leaf damage (%) at 7DAA
1	0.1	17
2	0	9
3	0.1	7
4	2.8	59

The death rate of *helicoverpa* due to abamectin alone was higher than anticipated in this trial, however addition of C1 or C1 plus EDTA reduced leaf damage by the insects.

#### Example 21cont: Compatibility of C1/EDTA with other insecticides.

(e) Carbaryl. Glasshouse trial. *Helicoverpa armigera* on geranium seedlings.

The potential of carbaryl as a co-insecticide with a mixture of C1plus EDTA was assessed by exposing *Helicoverpa armigera* larvae to the mixture and its

component parts in a glasshouse experiment. Geranium seedlings were prepared and treated as outlined in part d (above), except that the plants were sprayed with products outlined below.

1. Carbaryl (Arthur Yates Pty Ltd, 100g/L EC) applied at 1/100<sup>th</sup> the recommended rate for field use (10mL/L). A previous dose titration had indicated that this dilution was likely to give a sub-lethal response.
2. C1 (25mM) plus EDTA (disodium, 25mM).
3. C1 (25mM) plus EDTA (25mM) plus carbamate (0.1mL/L).
4. Untreated Control.

Assessments the total number of live, viable and active (TLVA) larvae, together with a subjective assessment of the percentage damage to leaves of each plant was made on day 7 after application (7DAA).

## RESULTS

- 15 Influence of the treatments on development of the population of *Helicoverpa* spp. over the trial period is illustrated in Table 21.5.

**Table 21.5. Insecticidal activity of carbaryl combinations.**

Code	Mean number of larvae / leaf at 7DAA	Estimated leaf damage (%) at 7DAA
1	1.20	41
2	1.45	41
3	0.60	23
4	2.25	65

20 The results indicate the insecticidal performance of a C1/EDTA mix can be improved by concurrent use of a low rate of carbaryl.